



**Centre de Ressources Biologiques-Tumorotheque:  
Bioresources and associated clinical data dedicated to  
translational research in oncology at the Institut de  
Cancérologie de l'Ouest, France**

Dominique Heymann, Estelle 4 Verhille, Vanessa 5 Veron, Marie 6 Vitre,  
Florian Delmas, Cécile Henry, Yann Gouy, Marie 10 Amiand, Jean-Marie Bard

► **To cite this version:**

Dominique Heymann, Estelle 4 Verhille, Vanessa 5 Veron, Marie 6 Vitre, Florian Delmas, et al..  
Centre de Ressources Biologiques-Tumorotheque: Bioresources and associated clinical data dedicated  
to translational research in oncology at the Institut de Cancérologie de l'Ouest, France. Open Journal  
of Bioresources, In press, Epub ahead of print. inserm-02529593

**HAL Id: inserm-02529593**

**<https://inserm.hal.science/inserm-02529593>**

Submitted on 2 Apr 2020

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

**Bioresource paper for submission to the *Open Journal of Bioresources***

To complete this template, please **replace the blue text with your own**. The paper has four main sections: (1) Overview; (2) Methods; (3) Bioresource description; (4) Reuse potential.

---

**(1) Bioresource Overview****Title**

Centre de Ressources Biologiques-Tumorotheque: Bioresources and associated clinical data dedicated to translational research in oncology at the Institut de Cancérologie de l'Ouest, France

**Paper Authors**

1. HEYMANN Dominique
2. KERDRAON Olivier
3. VERRIELE Véronique
4. VERHILLE Estelle
4. VERON Vanessa
5. VITRE Marie
6. DELMAS Florian
7. HENRY Cécile
8. GOUY Yann
9. AMIAND Marie
10. BARD Jean-Marie

**Paper Author Affiliations**

1. HEYMANN Dominique  
Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR  
Corresponding author: dominique.heyman@ico.unicancer.fr
2. KERDRAON Olivier  
Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR
3. VERRIELE Véronique  
Institut de Cancérologie de l'Ouest, 15 Rue André Boquel, 49055 Angers cedex 02, FR
4. VERHILLE Estelle  
Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR
5. VERON Vanessa  
Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR
6. VITRE Marie  
Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR
7. DELMAS Florian  
Institut de Cancérologie de l'Ouest, 15 Rue André Boquel, 49055 Angers cedex 02, FR
8. HENRY Cécile  
Institut de Cancérologie de l'Ouest, 15 Rue André Boquel, 49055 Angers cedex 02, FR

9. GOUY Yann

Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR

10. AMIAND Marie

Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR

11. BARD Jean-Marie 1. First author affiliation

Institut de Cancérologie de l'Ouest, Blvd Jacques Monod 44805 Saint-Herblain cedex, FR

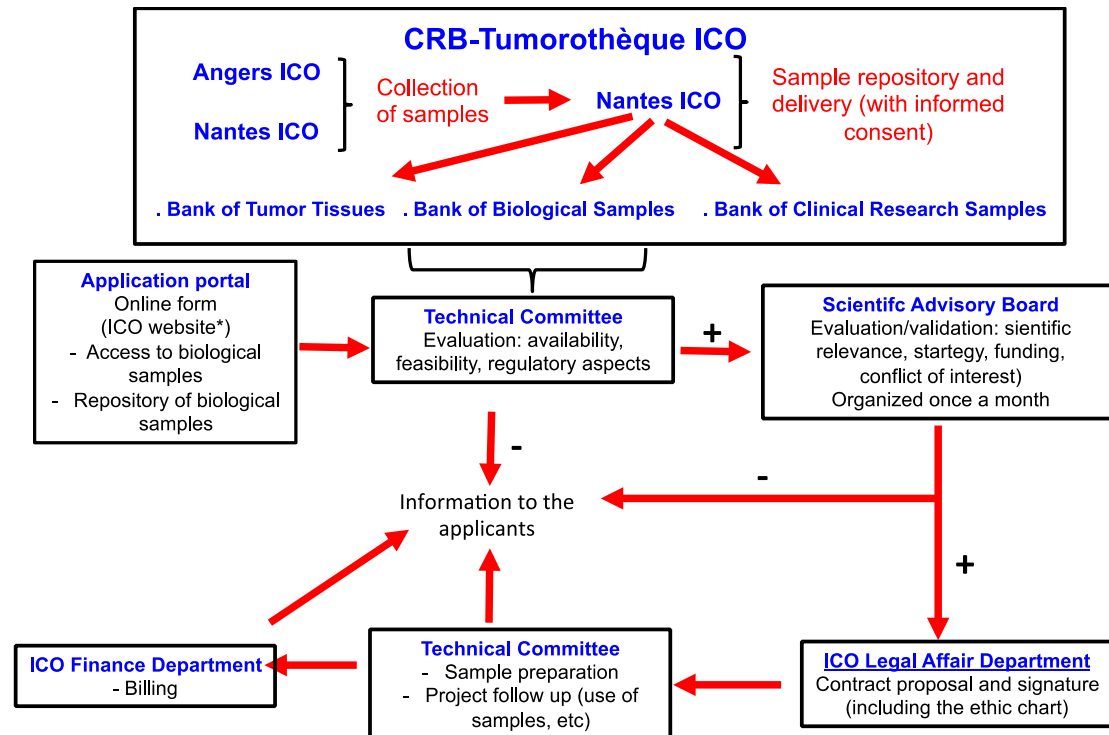
## **Abstract**

The Centre de Ressources Biologiques-Tumorotheque ICO is a biobank integrated in a clinical cancer center (ICO, Institut de Cancérologie de l'Ouest, Saint-Herblain, FR) that collects tissues (snap frozen, FFPE, TMA) and biological (serum, plasma, DNA, RNA, stools, etc) samples from oncology patients and dedicated to translational research. The biobank started its activities in 2002 and is certified NF S 96 900. Activities are framed by a quality management system with established and validated SOPs for all work procedures. Samples stored into the biobank are available for both academic as well as commercial researchers, through a defined access procedure. Currently the bioresources consist in more than 99.500 samples with informed consent and associated clinical data.

## **Project description**

The Centre de Ressources Biologiques-Tumorotheque ICO originates from the grouping of Tumor Bank of ICO created in 2002 located in Angers (FR) and biobank based at ICO Saint-Herblain (FR) created in 2003. The ICO biobanks initially shared with the University Hospital of Nantes was individualized from 1<sup>st</sup> July 2018 and became the CRB-Tumorotheque ICO. Samples are collected at both sites of the cancer center (Saint-Herblain and Angers), and the storage and delivery centralized at the Saint-Herblain site. The management of biocollection activities is carried out as part of a NF S 96 900 certification renewed in December 2018. The CRB-Tumorotheque ICO manages biological collections from multiple cancer types or collected in clinical trials in which ICO participates as a sponsor or through the physicians who are investigators. Eight biocollections entitled: breast-gynecology, genitourinary system, digestive system; nervous system; sarcomas; aerodigestive track; endocrinology; hematology are declared and registered under the reference DC-2018-3321.

The CRB-Tumorotheque is composed of three activity sectors: 1) "Tumor Tissue Bank" which collects tissue samples; 2) "biology" sector which collect biological samples and their derivatives other than tissues (e.g. blood, urine); 3) "clinical trials" sector collecting all samples related to clinical research protocols (Figure 1). The main objectives of the CRB-Tumorotheque are to ensure the traceability of all samples and associated processes to make them available to the scientific community for translational research projects.



**Figure 1: Organization of the CRB-Tumorothèque ICO and flowchart process.** Similar flowchart is required by the numeric data center to get access to clinical annotations. \* : <http://www.ico-cancer.fr/la-recherche/centre-de-ressources-biologiques-tumorotheque/>  
+: validation; -: rejection

### Classification (1)

Human

### Species

Human

### Classification (2)

Biological samples, biological samples and associated data, data only, clinical data

### Keywords

Tumor bank, cancer biospecimens, biobanking, Biological fluids, clinical data, translational research

### Context:

#### *Spatial coverage*

Description: Centre de Ressources Biologiques-Tumorotheque, Institut de Cancérologie de l'Ouest, Boulevard Jacques Monod, 44805 Saint-Herblain, cedex, France

Latitude: 47°14'16.4863"

Longitude: -1°38'15.2622"

***Temporal coverage***

Start from 2002 to present, no end date.

***Temporal coverage for accessibility:***

N/A: CRB-Tumorotheque ICO has no indicated date when bioresources must be destroyed.

## **(2) Methods**

### ***Steps***

#### ***1. Recruitment***

Patients diagnosed and treated at ICO for an oncologic disease who gave their agreement and have signed off the informed consent are eligible for the CRB-Tumorotheque. Patients are included at all clinical Departments. Biological resources can be also collected from external clinical centers and are couriered by certified transporters to the CRB-Tumorotheque ICO within an adequate period of time according the nature of bioresources.

#### ***2. Collection of bioresources***

Each clinical/surgical department of ICO collects biological samples in a uniform way and in a routine clinical care setting. Standard Operating Procedures have been established and validated for all laboratory methods related to the bioresources. Each process used at the CRB-Tumorotheque ICO integrates: staff education and training, safety procedures, access to the facility, logistics, identification of equipment/device and consumables, temperature control, document control, consent procedures, sample intake, handling, storage and distribution (SOPs), services, non-conformities, audit and management review. All these information/procedures are documented in a quality management system under supervision of the quality manager.

A request form including patient identification, material collected, date and time of the collection, informed consent is joined to the resource. Biological samples without informed consent are not processed.

All biological materials sent to the CRB-Tumorotheque ICO are delivered as fast as possible to guaranty the quality of the biological samples.

#### ***3. Preparation/transformation of bioresources***

Biological fluids and derivates, and tissue samples are processed by trained and certified staff through the biopathology department (histopathology and biology departments). Tissue specimens are validated by certified pathologists. Only surplus material is passed to the CRB-Tumorotheque ICO.

Immediately after receipt, samples are registered thanks the TumoroteK software, de-identified and processed according to the corresponding procedures. All steps of the process are documented into TumoroteK system. Tissue samples are stored as frozen or

Formalin-Fixed Paraffin-Embedded (FFPE) material. Biological fluids (e.g. urines, stools) and derivatives (e.g. plasma, serum, DNA, RNA) are aliquoted and stored at -80°C.

Only trained staff of the CRB-Tumorothèque ICO has access to the databases and the physical collections. In close collaboration with the numeric data center, staff has access to other databases of the ICO cancer center to retrieve clinical data, associated with the patient.

### ***Stabilization/preservation***

#### **Tissue**

- Formalin fixation and paraffin embedding
- Snap freeze tissues in isopentane and/or liquid nitrogen

#### **Serum**

- With or without clot activator (blood to clot in an upright position for at least 30 minutes but not longer than 1 hour before centrifugation)

#### **Plasma**

EDTA : centrifuged EDTA blood within 30 minutes

#### **Cells**

- Buffy coat: centrifuged EDTA/ACD blood at reception
- Peripheral Blood Mononuclear Cells: EDTA blood and Ficoll preparation
- Circulating Tumor cells [Cell-Free DNA BCT (Strek, USA) or Cell Save tubes (Silicon Biosystem/Menarini, Italy)]

#### **cfDNA**

- PAXgene Blood ccfDNA tube (Quiagen, France)

### ***Type of long-term preservation***

All bioresources prepared (Formalin Fixed Paraffin Embedded, frozen and cryogenic preserved samples). Preservation in access-controlled and temperature monitored facility.

### ***Storage temperature***

Depending on the bioresource:

- FFPE samples at room temperature (18-25°C)
- Snap freeze tissues at -80°C
- Serum, plasma and cfDNA at -80°C
- Cells at -196°C (liquid nitrogen)

### ***Shipping temperature from patient/source to preservation or research use***

Room temperature (18-25°C)

***Shipping temperature from storage to research use***

Depending on the bioresource:

- . Room temperature: FFPE samples
- . -80°C (on dry ice) (DNA, Plasma, Serum, Cells)

***Quality assurance measures***

All activities are carried out according to the French National Cancer Institute (INCa) recommendations [1-3].

Samples are processed according to Standard Operating Procedures by trained and qualified staff. All process steps are recorded into the TumoroteK (TK) data manager system which automatically generates an anonymization code for each sample linked to each biocollection. The measures established for ensuring the quality of samples include:

- Suitability of reagents for the sample processing and use of controlled/monitored laboratory materials.
- Procedure of intervention in case of an electrical blackout to safeguard samples with adequate alarm systems for frozen devices.
- Setting up of a risk-management storage system for each sample in separate freezers.
- Maintenance of the database up-to-date.
- Quality controls: e.g. DNA/RNA quantification and integrity validated by DNA/RNA Integrity Number (DIN/RIN) assessment
- Specific procedure for sample release: location check, quality sample check (volume, number of samples/amount of aliquots requested, anonymization code). In addition, for each tissue sample, a FFPE- or cryo-section is prepared, staining with Hematoxylin and Eosin and evaluated by a certified pathologist before transfer to the researcher. Diagnostic is then confirmed and if requested tumor cell percentage is determined.

The CRB-Tumorothèque ICO is certified NF S 96 900 («Quality of biological resource centres (BRCs) - Management system of a BRC and quality of biological resources») for the following activities: “Receipt, preparation and provision of cancer biological resources (tissues, fluids) from the tumor bank”.

***Source of associated data***

The demographical information (Gender, age) and clinical information (pathology report, treatment protocols, imaging, biological parameters, clinical follow up, etc) are available upon a specific request to the numeric data center associated with the CRB-Tumorothèque ICO and validation by the scientific advisory board.

***Ethics Statement:***

The activities of the CRB-Tumorothèque ICO are in accordance with the French legislation (especially the law of bioethics, 7<sup>th</sup> July 2011, and the chapter IV of the Public Health Code that gather all regulations for biobanks). They meet the ethical and regulatory requirements that govern the collection, conservation and use of biological samples for scientific purposes; this includes, according to article L.1243-3 of the Public Health Code, approval of the collection from a competent research

ethics committee (CPP, “Comité de protection des personnes” in French) and obligation to respect donor's informed consent in any access request to the samples. In addition, the CRB-Tumorotheque ICO works in respect to the national ethical chart reedited in 2010 [4]. All samples processed by the CRB-Tumorotheque ICO were subject to the donor's agreement and the signing of informed consent. The CRB-Tumorotheque is committed to destroying samples and related information at the request of the donor.

Researchers who would like to get access to bioresources available at the CRB Tumorotheque ICO must be compliant with the applicable law regarding their research projects and present legal/ethical authorisations/approvals required to the CRB upon request as a condition for granting access. As part of the access process, in addition to assessment of compliance with ethical and legal requirements, requests for assignments and accommodation are analysed on the relevance of scientific projects after validation by the scientific advisory board. All bioresources deposited at CRB-Tumorotheque ICO have been declared to and authorized by the French Research Ministry (Declaration Number: DC-2018-3321). This declaration includes approval by a research ethics committee (CPP).

### ***Constraints***

Available bioresources are composed by residual samples from patients who gave their agreement and have signed off the informed consent. External bioresources can be hosted by the CRB-Tumorotheque ICO upon request and validation by the scientific advisory board.

## **(3) Bioresource description**

### ***Object name***

Centre de Ressources Biologiques – Tumorotheque ICO

### ***Bioresource name***

Centre de Ressources Biologiques – Tumorotheque at the Institut de Cancérologie de l'Ouest

Bioresource acronym: CRB-Tumorotheque ICO

### ***Bioresource location***

Institut de Cancérologie de l'Ouest  
Boulevard Jacques Monod  
44805 Saint-Herblain  
France

### ***Bioresource contact***

CRBICO@ico.unicancer.fr



**Bioresource URL**

<https://www.institut-cancerologie-ouest.com/qualite-et-securite-des-soins#crb-tumorotheque182>

**Identifier used**

N/A

**Bioresource type**

CRB-Tumorotheque ICO is a clinical biobank dedicated to the preservation of biological samples from oncology patients.

**Type of sampling**

Biobank including Disease-based samples, longitudinal cohort, sampled in a research protocol

**Anatomical site**

Tissues and biological fluids from various tumor types and anatomical site are available.

**Disease status of patients/source**

Oncological patients.

**Clinical characteristics of patients/source:**

Adult and pediatric tumor samples with full clinical data de-identified before release. Clinical data are associated to each biological sample. Their access requests a specific application to the numeric data center associated with the CRB-Tumorotheque ICO and a validation by the scientific advisory board which serves as a formal Institutional Review Board.

**Size of the bioresource**

CRB-Tumorotheque ICO is a research infrastructure of the Institut de Cancérologie de l'Ouest dedicated to translational research and all collections are ongoing and have no definite end date. The collections contain currently (January 2020) around 100.000 biological samples originating from different research projects in collaboration with multiple researchers and physicians and are enriched by around 10.000 new samples each year.

**Vital state of patients/source**

Patients are alive at the time of sample collection. Patients are the source of clinical diagnoses.

**Clinical diagnosis of patients/source**

Eight biocollections are identified: Breast-Gynecology; Genitourinary system; Digestive system; Nervous system; Sarcomas; Aerodigestive track; Endocrinology; Hematology.

***Pathology diagnosis***

Variable

ICD-O M8000/0-M9989/3

***Control samples***

For tissue samples of the same organ both tumor and tumor-free tissue material macroscopically assessed are collected when possible.

***Biospecimen type***

CRB-Tumorotheque ICO can provide a large variety of biospecimens including serum, plasma, DNA, RNA, ascites, FFPE and fresh frozen tissues and Tissue Microarrays.

***Size of the bioresource***

The number of full time employees working at the CRB-Tumorotheque ICO is 10.

***Release date***

Samples and data are available since the 1<sup>st</sup> July 2018 upon request.

***Access criteria***

For any research group, a formal brief application is required (objectives, short description of samples, methods, data needed, timetable, associated funding) (Figure 1). All applications are reviewed by the governance committees (technical committee of the CRB-Tumorotheque ICO that checks the feasibility of the project on the base of the sample availability and the scientific advisory board that takes the final decision of acceptance after analysis of the scientific relevance, project feasibility and conflicts of interests. Similarly, access to clinical annotations will require a formal application and the validation of the numeric data center as well as the scientific advisory board of ICO. After acceptance, a contract including the ethical chart and the conditions of release will be proposed to the applicants and sign off before sample processing (e.g. conditions of transfer, storage, use, publication of results, disposal of withdrawn material, and financial aspects). The financial contribution is determined with the applicants and depends on the number and nature of data/samples needed as well as the nature of the contract (e.g. collaboration with shared publication or IP). In all cases, the origin of the materials provided (CRB-Tumorotheque ICO, FR) must be indicated in any communications done by the applicants.

***(4) Reuse potential***

The reuse by the contracting research group of samples delivered is not permitted without the permission of the CRB-Tumorotheque ICO. Conventionally, samples delivered in excess will be sent back to the CRB-Tumorotheque ICO for traceability and destruction. Tissue and fluid samples stored in multiple aliquots can be used for various projects.

## Acknowledgements

We would like to thank all members (pathologists, biologists, technicians) of the Biopathopathology Department (ICO, Saint-Herblain/Angers, FR) and steering committee for strategic decisions made to continuously develop the CRB-Tumorotheque ICO.

## Author Roles

1. HEYMANN Dominique - Head of the CRB-Tumorotheque
2. KERDRAON Olivier - Pathologist, Manager of the “Tumor Tissue Bank” sector
3. VERRIELE Véronique - Pathologist
3. VERHILLE Estelle - Technician of the Biobank
4. VERON Vanessa - Technician of the Biobank
5. VITRE Marie - Technician of the Biobank
6. DELMAS Florian - Technician of the Biobank
7. HENRY Cécile - Technician of the Biobank
8. GOUY Yann - Quality Manager
9. AMIAND Marie - Manager of the “Clinical Research” sector
10. BARD Jean-Marie - Manager of the “Biology” sector

## References

- [1] Plan Cancer, Mesure 20, Mesure 1. Soins et Recherche. Conservation et utilisation des échantillons tumoraux en cancérologie. Collection Référentiels & Recommandation. Indications 2011 de conservation et de cryoconservation à visée sanitaire. Recommandations pour l’organisation des tumorothèques et la constitution de collections biologiques à des fins de recherche en cancérologie. November 2011. <https://www.e-cancer.fr/>
- [2] INCa, Les tumorothèques hospitalière – Recommandations à l’usage des cliniciens et des chercheurs – November 2006 – <https://www.e-cancer.fr/>
- [3] Chassang G, Cambon-Thomsen A, Rial-Sebbag E. Éthique et réglementation des biobanques de recherche. Aspects opérationnels et perspectives. « Further readings explaining ethico-legal framework applied to French biobanks”. 2016. Ed. Biobanques. 231p. [http://www.biobanques.eu/files/Ethique%20et%20reglementation/Biobanques\\_GuideEthique.pdf](http://www.biobanques.eu/files/Ethique%20et%20reglementation/Biobanques_GuideEthique.pdf)
- [4] INCa- Charte éthique des tumorothèques – Edition 2010 – <https://www.e-cancer.fr/>

## Copyright Notice

Authors who publish with this journal agree to the following terms:

Authors retain copyright and grant the journal right of first publication with the work simultaneously licensed under a Creative Commons Attribution License that allows others

to share the work with an acknowledgement of the work's authorship and initial publication in this journal.

Authors are able to enter into separate, additional contractual arrangements for the non-exclusive distribution of the journal's published version of the work (e.g., post it to an institutional repository or publish it in a book), with an acknowledgement of its initial publication in this journal.

By submitting this paper you agree to the terms of this Copyright Notice, which will apply to this submission if and when it is published by this journal.